SM

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/079,035 | 02/19/2002 | John Andrew Ryals | 21212C | 7909 |

22847 7590 08/04/2004

SYNGENTA BIOTECHNOLOGY, INC.
PATENT DEPARTMENT
3054 CORNWALLIS ROAD
P.O. BOX 12257
RESEARCH TRIANGLE PARK, NC 27709-2257

| EXAMINER | |
|---|---|
| KUBELIK, ANNE R | |
| **ART UNIT** | **PAPER NUMBER** |
| 1638 | |

DATE MAILED: 08/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

SM.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/079,035 | RYALS ET AL. | |
| | Examiner | Art Unit | |
| | Anne R. Kubelik | 1638 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *25 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *33-36,39,40 and 42-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-36,39,40 and 42-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. Claims 33-36, 39-40 and 42-46 are pending.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The objection to claim 43 because of informalities is withdrawn in light of Applicant's amendment to the claim.

4. The rejection of claims 37-38 under 35 U.S.C. 101 as claiming the same invention as that of claims 2-3 of prior U.S. Patent No. 6,091,004 is obviated by their cancellation.

5. The rejection of claims 33-46 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention is withdrawn in light of Applicant's amendment of the claims.

6. The rejection of claims 45-46 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps is withdrawn in light of Applicant's amendment of the claims.

7. The rejection of claims 33-36, 39-40 and 42-46 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 5,986,082 is withdrawn in light of Applicant's amendment of the claims.

### *Claim Rejections - 35 USC § 112*

8. Claims 33-36, 39-40 and 42-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in

the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Neither the instant specification nor the originally filed claims appear to provide support for the phrase "An isolated DNA molecule that encodes a NIM1 protein comprising an amino acid sequence that has at least 99% identity to SEQ ID NO:3". Thus, such a phrase constitutes NEW MATTER. In response to this rejection, Applicant is required to point to support for the phrase or to cancel the new matter.

In the response filed 25 May 2004, Applicant urges that Table 5 describes a DNA sequence that encodes a protein with 99% identity to SEQ ID NO:3 (response pg 6).

This is not found persuasive because Table 5 does not describe a DNA sequence encoding a protein with 99%identity to SEQ ID NO:3. Table 5 compares the sequence to that of SEQ ID NO:1, which encodes the NIM1 protein on the opposite strand from that given. Figure 5D indicates that the coding region of SEQ ID NO:1 runs from nucleotide 3874 to nucleotide 1694. One of the "amino acid substitutions" in the WS sequence in Table 5 occurs at nucleotide 1607, which Figure 5D indicates is after the last codon of the gene. How this is possible is not described; thus, the sequence of the claimed DNA molecule is not described.

Furthermore, even if position 1607 were within the coding sequence, the protein has 5 amino acid substitutions and one deletion in a 594 amino acid long protein; this would not be an exact 99% identity, and there is no support for rounding the calculation.

9. Claims 33-36, 39-40 and 42-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids of SEQ ID NO:2 or encoding SEQ ID NO:3, plants transformed with them, and a method of using them to increase SAR gene

expression or enhance disease resistance in a transgenic plant, does not reasonably provide enablement for nucleic acids that encode a protein with 99% identity to SEQ ID NO:3, plants transformed with them, and a method of using them to increase SAR gene expression or enhance disease resistance in a transgenic plant. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is modified from the rejection set forth in the Office action mailed 26 November 2003, as applied to claims 33-36 and 39-46. Applicant's arguments filed 25 May 2004 have been fully considered but they are not persuasive.

The claims are broadly drawn to isolated DNA molecules that encode NIM1 proteins with 99% identity to SEQ ID NO:3. The claims are also drawn to plants transformed with those DNA molecules and methods of using those DNA molecules to increase SAR gene expression and enhance disease resistance in a plant.

The instant specification, however, only describes mutation of Arabidopsis plants and isolation of *nim* mutant plants that did not have resistance to *Peronospora parasitica*, even when sprayed with SA, INA or BTH, in comparison to NahG plants (examples 1-3); northern analysis of Pr-1, -2 and -5 gene expression in the mutant plants (example 4); analysis of SA accumulation (example 5); genetic analysis of the mutants to show that the mutants fell into t two complementation groups (example 6), mapping the NIM1 locus and isolation of the NIM1 gene, SEQ ID NO:1 (examples 7-11); determination of the mutations in the other mutants and the sequence of the gene in the Ws ecotype of Arabidopsis (example 12); complementation and Northern analysis to confirm that this gene corresponds to the mutation (example 13-14), isolation of the NIM1 cDNA (SEQ ID NO:2) (example 15); transformation of plants with

constructs comprising the NIM1 gene to show that they had increased resistance to pathogens (examples 18-19). The specification also prophetically discusses the isolation of homologous genes from other plants (example 17); generation of NIM1 deletion fragments (example 20), assessment of the CIM1 phenotype of the transformants (example 21), transformation of crop plants (example 22); use of *nim* mutants in crop and disease resistance testing, plant-pathogen interaction research, and fungicide screening (example 23-26).

The instant specification, however, fails to provide guidance for making isolated DNA molecules DNA molecules that encode NIM1 proteins with 99% identity to SEQ ID NO:3, and thus fail to provide guidance for plants transformed with those DNA molecules and methods of using those DNA molecules to increase SAR gene expression and enhance disease resistance in a plant.

Making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). All these mutated proteins, however, would have 99% identity to the original protein.

The specification fails to teach how to assay nucleic acids that encode proteins with 99% identity to SEQ ID NO:3. The recited function of the proteins encoded by these nucleic acids is that they are involved in the signal transduction cascade leading to SAR in plants and that they are inducible by INA. Many different proteins are involved in this process and they each have a different activity. Ryals et al (1996, Plant Cell 8:1809-1819) review a number of mutants that are involved in the signal transduction pathway leading to SAR (Figure 2); because these mutants complement one another, the genes must each encode a protein with a different activity. Similarly, Ward et al (1991, Plant Cell 3:1085-1094) teach that the expression of at least nine genes is induced in the SAR response (pg 1088, right column, paragraph 2); because their expression is induced, they are also involved in the signal transduction pathway. Thus, there is no single function for nucleic acids "involved in the signal transduction cascade leading to systemic acquired resistance in plants" and it is unclear how to assay the claimed nucleic acids. Furthermore, induction by INA is a function of the promoter, not a function of the protein itself.

As discussed above, Table 5 does not teach a DNA sequence encoding a protein with 99% identity to SEQ ID NO:3. Table 5 compares the sequence to that of SEQ ID NO:1, which encodes the NIM1 protein on the opposite strand from that given. Figure 5D indicates that the coding region of SEQ ID NO:1 runs from nucleotide 3874 to nucleotide 1694. One of the "amino acid substitutions" in the WS sequence in Table 5 occurs at nucleotide 1607, which Figure 5D indicates is after the last codon of the gene. How this is possible is not taught; thus, the sequence of the claimed DNA molecule is not taught.

Claim 34 is drawn to a DNA molecule that encodes a NIM1protein with 99% identity to SEQ ID NO:3, wherein the DNA is from any dicot, and claim 36 is drawn to a DNA molecule that

encodes a NIM1 protein with 99% identity to SEQ ID NO:3, wherein the DNA is from any monocot. However, NIM1/NPR1 proteins isolated from corn, rice, and wheat have 38.3%, 41% and 39.1% identity to the Arabidopsis protein (Crane et al, 2004, US Patent 6,713,665, column 45, lines 55-67; Bougri et al, 2003, US Patent Application Publication 20003/0115631, Table 1), and a glance at the alignment of the Arabidopsis protein and the Nicotiana glutinosa NPR1 protein indicates that the latter has much less than 99% identity to the former (Bougri et al, 2003, US Patent Application Publication 20003/0115631, Figure 1). Furthermore, the NIM1 protein from another Arabidopsis cultivar has about 99% identity to SEQ ID NO:3, indicating an unexpectedly broader sequence variation within a single species. Thus, it is unlikely that any NIM1 protein 99% identity to SEQ ID NO:3 could be from any monocot or dicot other than Arabidopsis.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate isolated DNA molecules that encode NIM1 proteins with 99% identity to SEQ ID NO:3, plants transformed with those DNA molecules, and methods of using those DNA molecules to increase SAR gene expression and enhance disease resistance in a plant.

Applicant urges that the claim has been amended to claim DNA molecules that encode NIM1 proteins with 99% identity to SEQ ID NO:3, the specification enables the skilled person to isolate NIM1 proteins that are 99% identical to SEQ ID NO:3 and teach whether such proteins are inducible by INA; once such proteins are found, an finite number of DNA molecules will encode such a protein (response pg 6).

This is not found persuasive because induction by INA is a function of the promoter, not a function of the protein itself. Furthermore, the rest of the function recitation, "wherein said

induction leads to systemic acquired resistance in said plant" requires the protein be in a plant, not isolated.

10. Claims 33-36, 39-40 and 42-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is modified from the rejection set forth in the Office action mailed 26 November 2003, as applied to claims 33-36 and 39-46. Applicant's arguments filed 25 May 2004 have been fully considered but they are not persuasive.

The claims are broadly drawn to a multitude of nucleic acids that encode NIM1 proteins with 99% identity to SEQ ID NO:3. In contrast, the specification only describes a coding sequence from *Arabidopsis* that comprises SEQ ID NO:2. Applicant does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

Table 5 does not describe a DNA sequence encoding a protein with 99%identity to SEQ ID NO:3. Table 5 compares the sequence to that of SEQ ID NO:1, which encodes the NIM1 protein on the opposite strand from that given. Figure 5D indicates that the coding region of SEQ ID NO:1 runs from nucleotide 3874 to nucleotide 1694. One of the "amino acid substitutions" in the WS sequence in Table 5 occurs at nucleotide 1607, which Figure 5D indicates is after the last codon of the gene. How this is possible is not described; thus, the sequence of the claimed DNA molecule is not described.

The function recited of the proteins encoded by these nucleic acids is that they are involved in the signal transduction cascade leading to SAR in plants and that they are inducible by INA. Many different proteins are involved in this process and they each have a different activity. Ryals et al (1996, Plant Cell 8:1809-1819) review a number of mutants that are involved in the signal transduction pathway leading to SAR (Figure 2); because these mutants complement one another, the genes must each encode a protein with a different activity. Similarly, Ward et al (1991, Plant Cell 3:1085-1094) teach that the expression of at least nine genes is induced in the SAR response (pg 1088, right column, paragraph 2); because their expression is induced, they are also involved in the signal transduction pathway. Furthermore, induction by INA is a function of the promoter, not a function of the protein itself.

Hence, Applicant has not, in fact, described nucleic acids that that encode NIM1 proteins with 99% identity to SEQ ID NO:3 within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

Applicant urges that Table 5 describes a DNA sequence that encodes a protein with 99% identity to SEQ ID NO:3 (response pg 6).

This is not found persuasive because Table 5 does not describe a DNA sequence encoding a protein with 99%identity to SEQ ID NO:3, for the reasons indicated above.

***Double Patenting***

11. Claims 33-36, 39-40 and 42-46 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 6,091,004. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, *e.g.*, *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). The rejection is repeated for the reasons of record as set forth in the Office action mailed 26 November 2003, as applied to claims 33-36 and 39-46. Applicant's arguments filed 25 May 2004 have been fully considered.

Applicant request that, as the scope of the claims may change in the course of prosecution, that this rejection be held in abeyance (response pg 8).

This is granted.

12. Claims 45-46 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-32 of U.S. Patent No. 6,031,153. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, *e.g.*, *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). The rejection is repeated for the reasons of record as set forth in the

Office action mailed 26 November 2003. Applicant's arguments filed 25 May 2004 have been fully considered.

Applicant request that, as the scope of the claims may change in the course of prosecution, that this rejection be held in abeyance (response pg 8).

This is granted.

### *Conclusion*

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system

provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Anne R. Kubelik, Ph.D.
July 29, 2004

ANNE KUBELIK
PATENT EXAMINER